Journal of Chromatography, 350 (1985) 336–338
Elsevier Science Publishers B.V., Amsterdam — Printed in The Netherlands

CHROM. 18 137

Note

Determination of papaverine by capillary isotachophoresis

IVO VÁLKA, DANIELA WALTEROVÁ and VILÍM ŠIMÁNEK*
Institute of Medical Chemistry, Medical Faculty, University Palacký, S. Allende 3, 775 15 Olomouc (Czechoslovakia)
(Received August 26th, 1985)

Papaverine, an isoquinoline alkaloid derived from opium, is a potent vasodilator and smooth muscle relaxant, which is used alone or in combination with analgesics in many pharmaceutical preparations. The European[1], United States[2] and Czechoslovak Pharmacopoeias[3] recommend for the determination of papaverine titration with perchloric acid in non-aqueous solvents or extraction from alkaline media with chloroform, drying and weighing as the free base. These methods are non-selective and inapplicable to low levels of papaverine. Recently, the indirect determination of papaverine by atomic-absorption spectrometry[4] and several methods involving gas–liquid, high-performance liquid[5] and high-performance thin-layer chromatography[6] has been reported. All these methods are time consuming.

Rapid isotachophoretic (ITP) methods have been developed for the direct determinating electrolyte β-alanine ($2 \cdot 10^{-2}$ *M*). Polyvinyl alcohol (0.5 g/l) was used paverine in some pharmaceutical preparations.

EXPERIMENTAL

Apparatus

An isotachophoretic instrument with coupled columns and conductivity detectors (Developmental Laboratories and Workshops, University Palacký, Olomouc, Czechoslovakia) was used. The driving current on the pre-separation capillary (230 × 0.8 mm I.D.) was 150 μA and on the analytical capillary (250 × 0.3 mm I.D.) it was 50 μA. The volume injected was 5 μl and the analysis time was about 20 min.

Electrolyte system

The leading ion was K^+ (10^{-2} *M*), the counter ion acetate (pH 4.5) and the terminating electrolyte β-alanine ($2 \cdot 10^{-2}$ *M*). Poly(vinyl alcohol) (0.5 g/l) was used as an additive in the leading electrolyte.

Sample preparation

Disintegrated tablets containing *ca.* 30 mg of papaverine were dissolved in 100 ml 10^{-3} *M* HCl. The solution was mixed for 30 min, filtered and injected. When the standard additions procedure was applied, after dissolution 20 ml of 10^{-2} *M* papaverine solution were added to one of two identical samples and both samples

0021-9673/85/$03.30

were then treated as described above. Extraction was carried out according to ref. 2. Determination by titration was carried out according to ref. 1.

RESULTS AND DISCUSSION

For the analysis, a leading electrolyte system of pH 4.5 was used, which allows the determination of papaverine as a cation. We analysed aqueous solutions of drugs containing papaverine and the ITP method was compared with determination by titration (Table I).

TABLE I

DETERMINATION OF PAPAVERINE IN SOME PHARMACEUTICAL PREPARATIONS

Preparation	*Labelled active ingredients*	*Papaverine found (%)*	
		ITP method	*Titration metho*
Papaverin tablets (I)*	Papaverinium chloratum, 40 mg	103.0 ± 1.7	99.7 ± 0.7
Papaverin injection (II)*	Papaverinium chloratum, 60 mg per 2 ml	101.7 ± 0.6	96.5 ± 1.7
Panergon capsule (III)**	Papaverinium chloratum, 150 mg	102.0 ± 1.2	96.3 ± 1.9
Spasmoveralgin tablets (IV)*	Papaverinium chloratum, 30 mg; bromisovalum, 250 mg; aminophenazonum, 150 mg; coffeinum 50 mg; phenobarbitalum, 20 mg; codeinium dihydrogenphosphoricum, 15 mg; ephedrinium chloratum, 5 mg; atropinium methobromatum, 0.5 mg	100.2 ± 2.3	888.6 ± 0.5***
Spasmoeunalgit tablets (V)*	Papaverinium chloratum, 50 mg; aminophenazonum, 220 mg; allobarbitalum, 30 mg; radobelinum, 0.1 mg	98.4 ± 2.5	737.4 ± 1.8***
Sedobelin dragée (VI)*	Papaverinium chloratum, 20 mg; phenobarbitalum, 50 mg; radobelinum, 0.25 mg	99.0 ± 0.9	385.5 ± 2.2***

* SPOFA, Czechoslovakia.
** Mack, F.R.G.
*** Sum of bases calculated as the content of papaverine.

At the selected pH of the leading electrolyte, even other alkaloids and aminophenazone migrated as cations. All of them formed sharp zones suitable for quantification. The isotachopherogram of a combined pharmaceutical preparation (Spasmoveralgin tablet IV) is shown in Fig. 1 as a typical isotachophoretic separation with the possibility of a parallel determination of several components. For the determination of papaverine, a calibration graph was mostly used. In some combined preparations (IV and V), in aqueous solution quantitative release of papaverine from the disintegrated tablet did not take place. In such instances, satisfactory precision and accuracy of the analysis were achieved by using the standard additions technique or by extraction of the tablets prior to ITP.

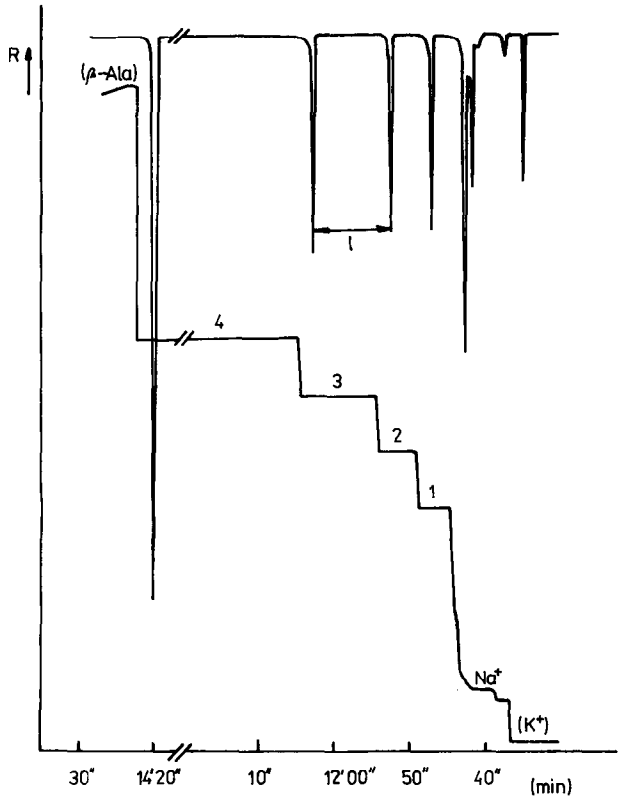

Fig. 1. Isotachopherogram of Spasmoveralgin tablets. 1 = Ephedrine; 2 = codeine; 3 = papaverine; 4 = aminophenazone.

In comparison with the standard method of papaverine determination, the ITP method has the advantages of offering high sensitivity and good selectivity.

REFERENCES

1 *European Pharmacopoeia*, Maisonneuve, Moulins les Metz, 1969, p. 360.
2 *Pharmacopeia of The United States of America*, XIX Revision, U.S. Pharmaceutical Convention, Rockville, MD, 1974, p. 745.
3 *Czechoslovak Pharmacopoeia*, III Revision, Avicenum, Prague, 1970, p. 953.
4 C. Nerin and A. Garnica, *Anal. Chem.*, 57 (1985) 34.
5 R. Verpoorte and A. B. Svendsen, *Chromatography of Alkaloids. Part B: Gas–Liquid Chromatography and High-Performance Chromatography*, Elsevier, Amsterdam, 1984.
6 J. de Schutter, B. Van der Weken, W. Van der Bossche and P. Moerloose, *Proc. Intern. Symposium on TLC with Special Emphasis on OPLC, Szeged, Sept. 10–14, 1984*, No. 24-25.
7 H. Klein and R. Teichmann, *Pharm. Ztg.*, 127 (1982) 447.
8 I. Válka, D. Walterová, M. E. Popova, V. Preininger and V. Šimánek, *Planta Med.*, (1985) 319.